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EXAMINER	
HOWARD, ZACHARY C	

ART UNIT	PAPER NUMBER
1646	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/051,843	WILLSON ET AL.	
	Examiner	Art Unit	
	Zachary C. Howard	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 July 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 7-52* is/are pending in the application.

4a) Of the above claim(s) *11-24,26,27 and 31-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 7-10, 25, 28-30 and 36-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1,2 and 7-52* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendments received by the Office on 6/20/01, 11/20/01, 1/11/02 and 7/11/03 have each been entered in full.

It is noted that the response received 1/11/02 was actually mailed by Applicants 11/8/01. The supplemental response of 11/20/01 was sent by fax. Therefore, the Office received and processed the 11/20/01 supplemental response prior to receiving and processing the first response that was mailed 11/8/01 but received 1/11/02. However, the Examiner has considered the responses in the order intended by Applicant.

To clarify:

The last Office Action was mailed to Applicants 5/20/01. The following responses have been received and considered:

1) The response received 6/20/01, which submitted a substitute sequence listing and amendments to the specification, in order to comply with the sequence requirements.

2) The response received 1/11/02 (but mailed 11/8/01), which amended claims 1, 2, 7, 8, 10, 25, 28-30, and added new claims 36-51.

3) The response received 11/20/01 by fax, which amended claims 38, 41-44, and 48-51, and added new claim 52.

4) The response received 7/11/03, which submitted, a substitute sequence listing and amendments to the specification, in order to comply with the sequence requirements.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This application contains claims 11-24, 26, 27 and 31-35 drawn to an invention nonelected with traverse in Applicant's response filed 1/10/2000. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claims 1, 2, 7-10, 25, 28-30 and 36-52 are under consideration.

Advisory Information

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) before the application can be examined under 35 U.S.C. §§ 131 and 132.

The instant specification will need to be amended so that it complies with 37 C.F.R. § 1.821(d) which requires a reference to a particular sequence identifier (SEQ ID NO:) be made in the specification and claims wherever a reference is made to that sequence. For rules interpretation Applicant may call (703) 308-1123. See M.P.E.P. 2422.04.

Claims 48-51 are not in compliance with 37 C.F.R. § 1.821(d).

Each of claims 48-51 refers to specific nucleotide residues (e.g., claim 48 recites "nucleotides 136-1095") but none of the claims contain a reference to the specific sequence identifier in which these nucleotides are found. These residues must have a reference point which would be a specific protein identified by SEQ ID number in each of these claims.

Applicant's cooperation is requested in correcting any other sequence references in the specification or claims that do not include a sequence identifier, and that Applicant becomes aware of.

Priority

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d) based on applications filed in Australia on 10/23/95, 12/22/95, and 9/9/96 numbered PN-6135, PN-7276, and PO-2208. The Examiner notes that a certified copy of each of these applications was submitted by Applicants 3/24/2003.

Withdrawn Objections and/or Rejections

The following page numbers refer to the previous Office Action (5/8/2001).

The objection to claim 30 at pg 3 for being a multi-dependent claim dependent on another multi-dependent claim is withdrawn in response to Applicants' amendments to the claims 1/11/02.

The objection to the claims (specific claim numbers were not specified) at pg 3 for encompassing the non-elected invention of SEQ ID NO: 1 is withdrawn in response to Applicants amendments to the claims 1/11/02.

The rejection of claims 1-2, 7-10, 25 and 28-30 under 35 U.S.C. § 112, second paragraph as being indefinite is *withdrawn* as follows:

Claims 1-2, 7-9, 28 and 29 were held indefinite for reciting "a derivative of said receptor". This is *withdrawn* in response to Applicants arguments. The phrase is broad but not indefinite.

Claim 29 was also held indefinite for reciting "comprises an amino acid sequence derived from IL-4 receptor α-chain". Applicants do not appear to address this argument in their response; however, the rejection is *withdrawn* as the phrase is broad but not indefinite.

Claims 28 and 29 were held indefinite because the metes and bounds of the term "interacts" could not be determined. This rejection is *withdrawn* in view of Applicants amendments to the claims to recite "binds".

Claim 7 was held indefinite because the "low stringency condition" were not specified. This rejection is *withdrawn* in view of Applicants amendments to the claim to include the specific low stringency conditions that are disclosed on pg 39, line 27 of the specification.

Claims 2, 7, 10 and 29 were held indefinite because the metes and bounds of term "capable of..." could not be determined. This rejection is *withdrawn* in view of Applicants amendments to the claim to remove the words "capable of".

Claim 30 was rejected for depending on an indefinite base claim. This rejection is *withdrawn* in view of Applicants amendments to the base claims.

The rejection of claim 25 at pg 6-10 under 35 U.S.C. § 112, first paragraph for lacking enabling support is *withdrawn in part* in view of Applicants' amendments to the claim. Specifically, the rejection of claim 25 at pg 8-10 for lacking enabling support for a pharmaceutical composition is withdrawn in view of Applicants' deletion of the word pharmaceutical from claim 25.

Specification

Page 1 (form PTO-326) of the 5/8/2001 Office Action includes an objection to the specification but does not include an objection to the Drawings. However, pg 2 of the 5/8/01 Action indicates that the drawings remain objected to for informalities in the Brief Description of the Drawings and does not indicate an objection to specification. Each page should have indicated that the specification was objected to for informalities in the Brief Description of the Drawings. It is noted that Applicants have amended the specification in the 1/11/02 response to address these informalities. However, the objection to the specification is maintained because all of the parts of Figures 1 and 7 are still not identified clearly. The Brief Description of Figure 1 now refers to Figures 1A to 1F (six Figures). However, the Drawings submitted 4/22/98 contain seven figures relating Figure 1, labeled as follows: Fig. 1; Fig. 1(i); Fig. 1(ii); Fig. 1(iii); Fig. 1(iv); Fig. 1(v); and Fig. (vi). Similarly, the Brief Description of Figure 7 now refers to Figure 7A-J

(ten Figures); however, the Drawings submitted 4/22/98 contain eleven figures relating to Figure 7, labeled as follows: Fig. 1 and Fig. 7(i) through Fig. 7(x).

The specification should be amended to refer to, and describe, each of these Figures as labeled in the Drawings submitted 4/22/98.

Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 45 and 46 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 45 and 46, as written, do not sufficiently distinguish over cells that exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See Diamond v. Chakrabarty, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g. by insertion of "isolated" or "purified". See MPEP 2105.

Claim Rejections - 35 USC § 112, 1st paragraph, scope of enablement

Claims 1-2, 7-10, 25, 28-30, 36-52 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated DNA (SEQ ID NO: 3) encoding a hemopoietin receptor (IL-13rα) or the extracellular domain of the receptor, isolated host cells comprising SEQ ID NO: 3, does not reasonably provide enablement for other DNA, or for non-isolated host cells comprising SEQ ID NO: 3. The specification does not enable any person skilled in the art to which it pertains, or with

which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

It is noted that the claims that recite nucleic acids comprising "a nucleotide sequence as set forth in SEQ ID NO..." have been broadly interpreted to encompass smaller nucleotides that are found within the recited SEQ ID NO..."

With respect to claims 1-2, 7-10, 25, and 28-30, were rejected at pg 6-8 of the 5/8/2001 Office Action, because the specification does not provide enablement for nucleic acids other than SEQ ID NO: 3. This rejection is herewith applied to new claims 36-44 and 46-52.

Applicants' arguments (1/11/02) as they pertain to the rejection have been fully considered but are not deemed to be persuasive for the following reasons.

In the response dated 1/11/02 Applicants at pg 11 submit the specification teaches the isolation and characterization of both murine IL-13rα (SEQ ID NOs: 1 and 2) and human IL-13rα (SEQ ID NOs: 3 and 4) using murine probes, and that the human and murine sequences have a high degree of sequence similarity. Applicants further submit the specification specifically describes sub-domains of IL-13rα and teaches preparation of soluble IL-13rα. Applicants argue that the Examiner admits that derivatives of IL-13 can be made according to the teachings of the specification, and that Applicants have identified specific functional derivatives and structural basis (sequences) from which said derivatives can be prepared.

Applicants' arguments have been fully considered but are not found persuasive. The Examiner agrees that the specification teaches isolation and characterization of murine and human IL-13Rα. The Examiner agrees that the specification teaches preparation of soluble murine IL-13Rα and that it could bind IL-13 (Example 12). The Examiner agrees that the specification describes several sub-domains of murine IL-13Rα including a signal sequence, transmembrane domain, extracellular domain (Thr37-Thr344), Ig-like domain (27-117) and haemopoietin receptor domain (118-340) (Examples 6 and 12). However, the Examiner disputes that these teachings enable the full scope "derivatives" of SEQ ID NO: 4 as encompassed by the claims. The term derivatives is not limited to fragments consisting of the extracellular domain of IL-13Rα,

which can bind IL-13, but instead broadly encompasses variants and fragments of SEQ ID NO: 4 in which one or more amino acids are substituted, deleted, and/or inserted. This includes fragments consisting of the aforementioned domains, none of which have been shown to bind IL-13 when prepared in isolation from the rest of the protein.

While some of the claims include the limitation that the polypeptide variants exhibit characteristics (ability to bind IL-13) of the parent polypeptide of SEQ ID NO: 4, the claims encompass an enormous scope of variants of SEQ ID NO: 4 in which any number of changes can be made to the sequence. Applicants do not disclose any actual or prophetic examples on expected performance parameters of any of the possible variants of polypeptides of SEQ ID NO: 4, other than a sole soluble receptor consisting of the entire extracellular domain of the protein. The specification has not provided a working example of the use of any other variants of the polypeptide of SEQ ID NO: 4, nor sufficient guidance so as to enable one of skill in the art to make such a variant. The specification has failed to teach which amino acids of SEQ ID NO: 4 could be modified so as to produce a polypeptide that is not identical to SEQ ID NO: 4 and yet still retain the activity of the polypeptide of SEQ ID NO: 4. The specification merely invites the skilled artisan to screen an extremely large genus of variants to determine whether or not each variant has the ability to bind IL-13.

Applicants have not given any guidance as to which amino acid substitutions, deletions or insertions to make to achieve any desired property, or defined a difference in structure, or difference in function, between the protein corresponding to SEQ ID NO: 4 and variants of said protein. If a variant of the protein corresponding to SEQ ID NO: 4 is to have a structure and function similar to the protein corresponding to SEQ ID NO: 4, then the specification has failed to teach one of skill in the art which amino acid substitutions, deletions or insertions to make that will preserve the structure and function of the protein corresponding to SEQ ID NO: 4. Conversely, if a protein variant of SEQ ID NO: 4 need not have a disclosed property; the specification has failed to teach how to use such a variant.

The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein

is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. Particular regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions [see Wells (18 September 1990) "Additivity of Mutational Effects in Proteins." Biochemistry **29**(37): 8509-8517; Ngo *et al.* (2 March 1995) "The Protein Folding Problem and Tertiary Structure Prediction, Chapter 14: Computational Complexity Protein Structure Prediction, and the Levinthal Paradox" pp. 492-495]. However, Applicants have provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions.

Although the specification outlines art-recognized procedures for producing variants, this is not adequate guidance as to the nature of active variants that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, it may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The art recognizes that function cannot be predicted from structure alone [Bork (2000) "Powers and Pitfalls in Sequence Analysis: The 70% Hurdle." Genome Research **10**:398-400; Skolnick and Fetrow (2000) "From gene to protein structure and function: novel applications of computational approaches in the genomic era." Trends in Biotech. **18**(1): 34-39; Doerks *et al.* (June 1998) "Protein annotation: detective work for function

prediction." Trends in Genetics **14**(6): 248-250; Smith and Zhang (November 1997) "The challenges of genome sequence annotation or 'The devil is in the details'." Nature Biotechnology **15**:1222-1223; Brenner (April 1999) "Errors in genome annotation." Trends in Genetics **15**(4): 132-133; Bork and Bairoch (October 1996) "Go hunting in sequence databases but watch out for the traps." Trends in Genetics **12**(10): 425-427].

Due to the large quantity of experimentation necessary to generate the large number of derivatives recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

With respect to claims 30, 36, 45 and 46, these claims lack enablement because they are directed to a broad genus of host cells comprising an expression vector that, in turn, comprises the claimed DNA. The specification contemplates two subgenera in which such host cells can be made and used. Specifically, the specification contemplates making and using the host cells in culture and also in gene therapy. It is noted that claim 30 previously recited "an isolated and purified animal cell..." but was amended to recited "a host cell..." and therefore now encompasses a broad genus of host cells including those that are not isolated.

The specification asserts that host cells can be made and used in two contexts.

1) The specification contemplates making and using isolated host cells in culture to produce the encoded protein recombinantly. Such is enabled, since the specification and prior art provide specific guidance on how to make and use host cells for this purpose. Undue experimentation would not have been required of the skilled artisan to make and use the claimed host cells in this context.

2) The specification also discloses that nucleotide constructs comprising the claimed gene can be used to genetically engineer host cells to express such products *in vivo* and that these products can be used in gene therapy approaches (pg 30, lines 16-21). However, the specification does not teach any methods or working examples that indicate the claimed nucleic acid is introduced and expressed in a cell for therapeutic purposes. The disclosure in the specification is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. For example, the specification does not teach what type of vector would introduce the claimed nucleic acid into the cell or in what quantity and duration. Relevant literature teaches that since 1990, about 3500 patients have been treated via gene therapy and although some evidence of gene transfer has been seen, it has generally been inadequate for a meaningful clinical response (Phillips, A., J Pharm Pharmacology 53: 1169-1174, 2001; abstract). Additionally, the major challenge to gene therapy is to deliver DNA to the target tissues and to transport it to the cell nucleus to enable the required protein to be expressed (Phillips, A.; pg 1170, ¶ 1). Phillips also states that the problem with gene therapy is two-fold: 1) a system must designed to deliver DNA to a specific target and to prevent degradation within the body, and 2) an expression system must be built into the DNA construct to allow the target cell to express the protein at therapeutic levels for the desired length of time (pg 1170, ¶ 1). Therefore, undue experimentation would be required of the skilled artisan to introduce and express the claimed nucleic acid into the cell of an organism to treat disease. Additionally, gene therapy is unpredictable and complex wherein one skilled in the art may not necessarily be able to introduce and express the claimed nucleic acid in the cell of an organism or be able to produce the encoded protein in that cell.

Due to the large quantity of experimentation necessary to introduce and express the claimed nucleic acid in a cell of an organism for therapy, the lack of direction or guidance presented in the specification regarding how to introduce the claimed nucleic acid in the cell of an organism to be able produce the encoded protein, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of transferring genes into an organism's

cells, and the breadth of the claims which fail to recite any cell type limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Please note that this issue could be overcome by amending the claims to recite, for example, "An isolated host cell..." because such an amendment would clarify that the claims are directed only to host cells which are to be made and used in culture as described in context 1) above.

Claim Rejections - 35 USC § 112, 1st paragraph, written description

Claims 1-2, 7-8, 10, 25, 28-30, 36-44 and 46-52 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The instant specification does not contain a written description of the invention in such full, clear, concise, and exact terms or in sufficient detail that one skilled in the art can reasonably conclude that applicant had possession of the claimed invention at the time of filing. This rejection was set forth at pg 10-13 of the 5/8/01 Office Action for claims 1-2, 7-8, 10, 25 and 28-30 and is herewith applied to new claims 36-44 and 46-52.

The claims encompass a genus of isolated nucleic acids encoding derivatives of a haemopoietin receptor (HR) of SEQ ID NO: 4, host cells comprising said nucleic acids, and methods of producing recombinant polypeptides.

The specification discloses isolated cDNAs having the sequence of SEQ ID NO: 1 and 3, which encode polypeptides having the sequence SEQ ID NO: 2 and 4. The claims, as written, however, encompass polynucleotides that vary substantially in length and also in nucleotide composition. The broadly claimed genus additionally encompasses polynucleotides that may be completely unrelated to the polynucleotide SEQ ID NOs: 1 and 3. For example, in claim 2, a "derivative" of SEQ ID NO: 1 or 3 that encodes a receptor capable of interaction with a derivative of IL-13 does not actually have any particular identity with SEQ ID NO: 1 or 3.

The instant disclosure of SEQ ID NOs: 1 and 3 does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of subgenera including full-length proteins, chimeric proteins, fusion proteins, allelic variants, and derivatives. The derivatives or variants may have no known or disclosed function. For example, in claim 2, a derivative of SEQ ID NOs: 1 or 3 that is capable of interaction with a derivative of IL-13 may be a protein completely unrelated to instant invention, structurally and functionally. The polypeptides, encoded by polynucleotides isolated by hybridization may be completely unrelated to the polypeptide of SEQ ID NOs: 2 or 4. Further, polypeptides, comprising fragments, may also be completely unrelated to the polypeptide of SEQ ID NOs: 2 or 4. A description of a genus of polypeptides may be achieved by means of a recitation of a representative number of polypeptides, defined by amino acid sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the claimed genus of polypeptides. There is no description of the conserved regions that are critical to the structure and function of the genus claimed. For example, what region or domain of the polypeptide of SEQ ID NO: 2 or 4 contains a definitive structural feature required for protein function? The specification proposes to discover other members of the genus by using screening assays and techniques involving probes, primers, or hybridization. There is no description, however, of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from others excluded are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polynucleotides encompassed. No identifying characteristic or property of the instant polypeptides is provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed. Since the disclosure fails to describe the common attributes or

characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of specific polypeptide and nucleotide sequences and the inability to screen, is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe, enable and use the genus as broadly claimed. For the reasons forth above, it does not appear that the inventors were in possession of the claimed derivatives and variants recited in claims 1-2, 7-8, 10, 25, 28-30, 36-44 and 46-52, at the time of filing.

Applicants' response (1/11/02) does not contain any response to this rejection, or acknowledgement of the rejection. Applicants' amendments to the claims have been fully considered, but do not overcome this rejection.

Claim Rejections - 35 USC § 112, 1st paragraph, new matter

Claims 38-44 and 48-51 are also rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement because the claims contain new matter.

Claims 38-51 were newly introduced in Applicant's response received 1/11/02 (but mailed 11/8/01 as noted above). Claims 38, 41-44, and 48-51 were amended in Applicant's supplemental response received 11/20/01. The Examiner can find no comments by Applicants in either response indicating where in the specification support for claims 37-51 can be found. It is noted that at pg 3 of the 11/20/01 response Applicants indicate that "Support for added claim 52 is found throughout the specification and particularly at Claim 38" but no support for claim 38 was previously provided.

Each new claim encompasses a genus of nucleic acids that does not have support in the specification as originally filed.

Claims 38-42 each encompass a genus of isolated nucleic acids comprising an extracellular domain of a haemopoietin receptor. Claim 38 encompasses a genus of isolated nucleic acids "comprising a sequence of nucleotides that encodes an extracellular domain of a haemopoietin receptor." This claim broadly encompasses any haemopoietin receptor (HR). The language used, i.e., "a sequence of nucleotides that

encodes an extracellular domain" indicates that the genus is not limited to any particular portion of an extracellular domain (ECD). Claims 39 and 40 each depend from claim 38 and limit the ECD to either an immunoglobulin-like domain (ID; claim 39) or an haemopoietin receptor domain (HRD; claim 40). Again, claims 39 and 40 broadly encompass any HR. Claim 41 depends from claim 39 and limits the ID to consisting essentially of amino acids 28-118 of SEQ ID NO: 4. Claim 42 depends from claim 40 and limits the HRD to consisting essentially of amino acids 119-341 of SEQ ID NO: 4.

The specification teaches the following regarding isolated nucleic acids encoding extracellular domains of hematopoietin receptors. The specification refers to soluble NR4 (IL-13Rα) on pages 7, 9, and 27. On page 27 the specification discusses uses of soluble IL-13Rα, e.g. to prevent interaction between IL-13 and NR4 (which is membrane bound). Page 37 discloses the characterization of the murine NR4, and teaches that the extracellular region of the protein of SEQ ID NO: 2 contain an immunoglobulin domain (amino acids 27-117), in addition to a typical haemopoietin receptor domain (amino acids 118-340). Page 40 teaches production of soluble murine IL-13Rα by using PCR primers specific for the DNA encoding the extracellular region from Thr27 to Thr344. The specification further provides an alignment between murine IL-13Rα and human IL-13Rα, showing strong homology between the extracellular domain (Thr27 to Thr344) of each protein.

As stated above, Claim 38 encompasses <u>any</u> extracellular domain from <u>any</u> hematopoietin receptor. In addition nucleic acids encoding full-length receptors, this genus encompasses nucleic acids comprising fragments consisting solely of extracellular domains. The specification teaches a single example of this, a nucleic acid consisting of the extracellular domain of SEQ ID NO: 2. Due to the strong homology between SEQ ID NO: 2 and 4, and the general teachings of the specification about soluble IL-13Rα, a nucleic acid consisting of the extracellular domain (Thr27 to Thr344) of SEQ ID NO: 4 would also flow naturally from the specification. However, there is no conception in the specification of a genus of isolated nucleic acid molecules comprising <u>any</u> extracellular domain from <u>any</u> hematopoietin receptor (HR). Nor does this genus

flow naturally from the disclosure of the specification. Therefore, the specification as originally filed lacks support for claims 38-40.

Claim 43, 44 and 48-51 each depend from claim 37. Claim 37 encompasses a genus of isolated nucleic acid molecules comprising a nucleotide sequence "as set forth in SEQ ID NO: 3". As noted above, this terminology is interpreted broadly to encompass all smaller nucleotide sequences found with a sequence of SEQ ID NO: 3. Claims 43, 44 limit the nucleic acid to those encoding, respectively, a polypeptide consisting essentially of amino acids 26-345 (claim 43) or 26-426 (claim 44) of SEQ ID NO: 4. Claims 48-51 limit the nucleic acid to a sequence consisting essentially of nucleotides 136-1095 (claim 48); 136-1338 (claim 49); 142-414 (claim 50); or 415-1083 (claim 51).

There is no conception in the specification of isolated nucleic acids consisting essentially of the recited regions, nor does the concept of each specific genus flow naturally from the disclosure of the specification. It is noted that the specification discusses nucleic acids comprising amino acids 27-344 (the extracellular domain) of IL-13Rα, but that there is nothing pointing to a specific region of 26-345, nor does this specific region flow naturally from the teachings of the specification. Therefore, the specification as originally filed lacks support for claims 43, 44 and 48-51.

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 52 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 52 is indefinite because it recites "the isolated nucleic acid molecule of claim 38 comprising the amino acid sequence set forth in SEQ ID NO: 4. It is unclear how a nucleic acid can comprise an amino acid sequence. In this regard, this would be

rendered definite if amended, for example, to recite "...nucleic acid molecule of claim 38 encoding the amino acid sequence..."

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 38-40 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Larsen et al, 1990, J. Exp. Med. 172: 1559-1570.

Claim 38 encompasses a genus of isolated nucleic acids "comprising a sequence of nucleotides that encodes an extracellular domain of a haemopoietin receptor." This claim broadly encompasses any haemopoietin receptor (HR). Claims 39 and 40 each depend from claim 38 and limit the ECD to either an immunoglobulin (Ig)-like domain; claim 39) or an haemopoietin receptor domain (HRD; claim 40). Again, claims 39 and 40 broadly encompass any HR.

Larsen teaches "the isolation from a placental library of two cDNA clones that encode high affinity receptors for G-CSF when expressed in COS-7 cells" (pg 1560). Larsen further teaches that the G-CSF extracellular region contains sequences with homology to "members of the Ig superfamily" and "the extracellular regions of all members of the recently identified hematopoietin (HP) receptor family" (pg 1564). Larsen further teaches isolated of mRNA encoding the receptor (see pg 1561). Therefore, the isolated mRNA encoding G-CSF receptor taught is an isolated nucleic acid molecule comprising a sequence that encodes an extracellular domain of a haemopoietin receptor, and this sequence also comprises an Ig-like domain and a haemopoietin receptor domain. Therefore, Larsen clearly anticipates instant claims 38-40.

Conclusion

No claims are allowed.

Applicants' amendments necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicants are reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary C. Howard whose telephone number is 571-272-2877. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 571-272-0829. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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